

Examiner considers claims 1-146 to be pending and claims 1-36 to be under consideration in the instant application. Applicants accordingly request reinstatement of original claims 20-36 and likewise request the Examiner to treat claims 1-36 as currently pending and under consideration in the instant application. No new matter is introduced by this amendment. Payment for claims 20-36 is enclosed with this Amendment and Response.

Amendments have been made to the specification in order to address the Notice of Draftsperson's Patent Drawing Review and the Objection to Specification which appears on page 3 of the Office Action. These amendments are non-substantive and do not add new matter to the application. Marked up versions of the replacement paragraphs and text are presented herewith on a separate sheet.

Drawing

New corrected drawings, corresponding to Figures 4, 5, and 9, are filed herewith in accordance with the Notice of Draftsperson's Patent Drawing Review and the Examiner's requirement of such correction as part of this response to Office Action. After review of the figures, it is not clear what the Draftsperson found objectionable about the margins for Figures 5 and 9. The corrections nonetheless consist of increasing margins on the figures.

Applicants also respectfully point out that the Examiner's reference to "The drawing (one figure only) filed 3 March 2000" appears to be in error. The recited date precedes the filing date of the instant application, and ten figures were filed with the application.

Objection to Specification

In response to the Objection to Specification appearing on page 3 of the Office Action, Applicants have amended the paragraph which appears on page 3, lines 4-14 of the specification to include the parenthetical "(PS A)" at the first occurrence of the spelled out term "polysaccharide A" in the specification on page 3. This amendment is intended to address objection (1) of the Examiner. Replacement in the specification of the paragraph which begins on page 35, line 28, and of the heading which appears on page 36, line 29 merely changes "PSA" to "PS A" in accord with objection (2) of the Examiner. Applicants request the Examiner to withdraw the Objection to Specification in view of the amendments made herewith.

Rejections Under 35 U.S.C. § 112, Second Paragraph

The Examiner has indicated that claims 1-36 are rejected as being indefinite. With respect to claims 1, 19, and claims which depend from claims 1 and 19, the Examiner has indicated first that polymer molecular weight "less than 50 kilodaltons" and separations described in terms of certain minimum distances (e.g., "separated by a distance of at least 8 amino acids") are indefinite. Applicants respectfully disagree with the Examiner's rejection on this basis because one of skill in the art would appreciate that the molecular weight and physical dimension limitations, as set forth concurrently in the claims, work together to delineate the lower and upper limits which apparently concern the Examiner. Because the polymer as claimed can encompass any of a variety of subunits of different molecular weights and physical

dimensions. Applicants have not arbitrarily selected particular cut-offs in either of these parameters. One of skill in the art, in selecting a particular polymer, would be able to determine whether the particular polymer meets the molecular weight and physical dimension limitations set forth in the claims.

With regard to point (ii) made by the Examiner in rejecting claims 1 and 19, Applicants agree with the Examiner that the quoted language "composed of ... a negative charge" does not alone describe the repeating charge motif. Rather, as a more full reading of the same claim language makes clear, the repeating charge motif is composed of "a positively charged free amino moiety and a negative charge" [emphasis added]. Thus a proper reading of the claim language does not reasonably suggest that the charge motif is composed of a single negative charge. Furthermore, one of skill in the art would recognize that, while indeed "a negative charge" may characterize a physiochemical feature of a charged molecule, the meaning of "a negative charge" is not indefinite in the context of the claim as a whole, which is directed to a pharmaceutical composition.

Turning to point (iii) made by the Examiner in rejecting claim 1, Applicants submit to the Examiner that the plain meaning of the recitation "separated by an intervening sequence of at least 32 Å" refers to the dimension occupied by the intervening molecular structure. Applicants thus respectfully request the Examiner to withdraw the rejection of claims 1 and 19 under 35 U.S.C. § 112, second paragraph.

The Examiner has also indicated that claims 3 and 4 are rejected under 35 U.S.C. § 112, second paragraph, for indefiniteness arising from use of the terms "repeating unit" and "identical repeating unit". As provided at page 20, lines 5-13 in the specification, the terms "repeating unit" and "identical repeating unit" have definite meaning. In contrast to the assertion made by the Examiner, "repeating unit", even when referring to charge motifs, can in fact limit claim 1. For example, in claim 1 the repeating charge motif can, but need not necessarily, be a repeating unit within the meaning of that term as defined in the specification. Thus the limitation in claim 3 that the polymer has repeating units can further limit claim 1 when, for example, the repeating charge motif is a repeating unit within the meaning of that term as defined in the specification. Of course the repeating unit can refer to either a charge motif or another aspect of the polymer, i.e., a "non-charge motif" (Examiner's terminology). Applicants thus respectfully request the Examiner to withdraw the rejection of claims 3 and 4 under 35 U.S.C. § 112, second paragraph.

The Examiner has also indicated that claim 7 is rejected under 35 U.S.C. § 112, second paragraph, for indefiniteness arising from use of the term "peptide-nucleic acid". As provided at page 19, lines 27-28 in the specification, the term "peptide-nucleic acid" refers to polymers having the requisite charge motif and a heterogeneous backbone composition in which there are "amino acids linked to nucleic acids". This definition thus clearly embraces both "amino acids [scattered] within a polynucleotide" and "a peptide fragment covalently linked to a polynucleotide". Applicants thus respectfully request the Examiner to withdraw the rejection of claim 7 under 35 U.S.C. § 112, second paragraph.

The Examiner has also indicated that dependent claims 8, 9-10, 13, 16, 17, 22-26, 28-30, and 33-34 are rejected under 35 U.S.C. § 112, second paragraph, for indefiniteness arising from use of the term "at least 10 (or 15 or 20) repeating charge motifs" (parenthetical added). Applicants respectfully submit that the number of motifs is definite insofar as claims 1 and 19, as pointed out above, set forth both molecular weight and physical dimension limitations that, taken together, set definite upper limits on the number of repeating charge motifs. This point is also addressed, for example, at page 21, lines 16-19 of the specification.

Finally, the Examiner has also indicated that claims 27 and 36 are rejected under 35 U.S.C. § 112, second paragraph, for indefiniteness arising from use of the term "any neural [sic] amino acids". Applicants intend amino acids to include both naturally-occurring and non-naturally-occurring amino acids. In making the rejection, the Examiner makes reference to naturally occurring amino acids Arg, Lys, Glu, Asp and His. Applicants respectfully submit to the Examiner that the specification identifies lysine (K), arginine (R), asparagine (N), and histidine (H) as examples of naturally-occurring positively charged amino acids and aspartic acid (D) and glutamic acid (E) as examples of naturally-occurring negatively charged amino acids. Such assignments are consistent with the well recognized meanings of those terms as used by persons skilled in the art. Thus Applicants do not mean to exclude any other amino acids, naturally-occurring or otherwise, from neutral amino acids. Furthermore, use of the term "neutral amino acid" in the specification is consistent with the well recognized meaning of that term as used by those of skill in the art.

In view of the foregoing, Applicants respectfully request the Examiner to withdraw the rejection of claims 1-36 under 35 U.S.C. § 112, second paragraph.

Rejections Under 35 U.S.C. § 103(a)

The Examiner has indicated that claims 1, 6, and 7 are rejected under 35 U.S.C. § 103(a) as being obvious over Simmons GC et al. (*Bioorg Med Chem Lett* (1998) 7:3001-6) taken with Basu S et al. (*Bioconjugate Chem* (1997) 8:481-8) and Nielsen PE (*Curr Opin Biotechnol* (1999) 10:71-5). Applicants respectfully disagree with the Examiner's rejection because the references, even if combined as suggested by the Examiner, neither teach nor suggest the claimed inventions, even with the benefit of hindsight. The Simmons reference teaches PNA-peptide conjugates which, as the Examiner correctly points out, appear to be less than 50 kDa and which have a multiplicity of positively charged amino acid residues. At a minimum, none of the four PNA-peptide conjugates disclosed in Simmons has at least two repeating charge motifs, each composed of a positively charged free amino moiety and a negative charge, as required by claim 1. Neither Basu nor Nielsen provides any teaching or motivation to arrive at the claimed subject matter of claims 1, 6, or 7. Rather, Basu and Nielsen at most teach only that PNAs in general (Nielsen) and certain PNA-peptide conjugates in particular (Basu) may be administered as therapeutics. Thus neither Basu nor Nielsen adds anything to Simmons to render obvious the subject matter of claims 1, 6, or 7. Furthermore, Basu and Nielsen taken together in combination with Simmons fails to render obvious the subject matter of claims 1, 6, or 7.

In view of the foregoing, the Applicants respectfully submit that the Examiner has failed to make a prima facie case for rejection of claims 1, 6, and 7 under 35 U.S.C. § 103(a) and thus request the Examiner to withdraw the rejection of claims 1, 6, and 7 made under 35 U.S.C. § 103(a).

Summary

Claims 20-36 are reinstated and claims 1-36 are under consideration in the instant application. Nonsubstantive amendments have been made to the specification to address the Objection to Specification and the Notice of Draftsperson's Patent Drawing Review. Arguments are presented in response to rejections made under 35 U.S.C. § 112, paragraph 2, and 35 U.S.C. § 103(a), and the Examiner is urged to withdraw all rejections.

Applicant believes the claims are in condition for allowance. A favorable action is earnestly solicited.

Respectfully submitted,



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MARKED UP VERSIONS OF REPLACEMENT TEXT

The CPC consists of two distinct high molecular weight polysaccharides, termed A and B. Each polysaccharide is composed of distinct oligosaccharide repeating units possessing uncommon constituent sugars with free amino, carboxyl and phosphonate groups. Polysaccharide A (PS A) has a tetrasaccharide repeating unit with a balanced positively charged amino group and negatively charged carboxyl group. Polysaccharide B has a hexasaccharide repeating unit, including an unusual 2-amino ethylphosphonate substituent containing a free amino group and negatively charged phosphate group. The galacturonic acid residue contains an additional negatively charged carboxyl group. Ionic interaction between the two saccharide chains tightly links polysaccharides A and B into the high molecular weight CPC complex. The complex capsular motif is a conserved trait for all strains of *B. fragilis* that have thus far been examined.

B. fragilis NCTC 9343 and ATCC 23745 were originally obtained from the National Collection of Type Cultures (London, England) or the American Type Culture Collection (Bethesda, MD). Microorganisms were stored at -80°C in peptone-yeast or brain heart infusion broth until used, and grown anaerobically as previously described. Pantosti et al. *Infect Immun* 59:2075 (1991). The CPC from *B. fragilis* NCTC 9343 or ATCC 23745 was isolated by hot phenol/water extraction and subsequent purification of [PSA] PS A performed as previously described. Tzianabos, A et al. *J Biol Chem* 267:18230 (1992).

T Cell Activation by [PSA] PS A Depends on Charge Motif